Primary choriocarcinoma of the urinary bladder

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PRIMARY CHORIOCARCINOMA OF THE URINARY BLADDER

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A 72-year-old woman with asymptomatic macrohematuria was referred to our hospital. Cystoscopy revealed a 7cm sessile tumor on the left lateral wall of the bladder. Subsequently an intravenous pyelography revealed left hydronephrosis. We performed transurethral biopsy and resection of the bladder tumor under the diagnosis of ordinary malignant bladder tumor. Histopathologically, the lesion was shown to be an undiffentiated urothelial carcinoma, G3, ≧pT2, containing syncytiotrophoblastic giant cells. The level of serum human chorionic gonadotropin-beta (hCG-β) level was slightly elevated (0.3 ng/ml ; normal value : $<$0.1). Because a further examination revealed an invasion into the surrounding fat tissue of the bladder and left ureter, a total cystohysterectomy with an ileal conduit were performed. The final histopathological classification was choriocarcinoma of the urinary bladder, pT3a, pN1, pMx. An adjuvant combination chemotherapy was carried out using methotrexate, vinblastine, adriamycin and cisplatin (MVAC). After two courses of chemotherapy, the serum hCG-β levels returned to normal. Eleven months postoperatively, however, there was evidence of multiple lung metastases. The patient died 12 months after the surgery as a result of complications caused by widespread metastases.

(Hinyokika Kiyo **54** : 293–296, 2008)

Key words : Bladder tumor, hCG-β, Choriocarcinoma

INTRODUCTION

Choriocarcinomas usually develop in the uterus and ovaries in the female, while being extremely rare in the urinary tract system. Their occurrence in the urinary tract is rare, especially in the bladder. To our knowledge, 36 cases of primary choriocarcinoma of the urinary bladder have been described in the world[1–4]. We report herein a female with this disease.

CASE REPORT

A 72-year-old woman was referred to our hospital in April 2005 for asymptomatic macrohematuria. She had no past medical history but her family history was not sufficiently taken. Cystoscopy revealed a 7 cm sessile tumor on the left lateral wall of the bladder. An intravenous pyelography revealed left hydronephrosis. The result of urinary cytology was Class III. We diagnosed the patient as having an invasive tumor of the urinary bladder. She underwent a transurethral resection of the bladder tumor. A histopathological examination showed an invasive undifferentiated carcinoma containing syncytiotrophoblastic giant cells. Magnetic resonance imaging (MRI) revealed an irregularly thickened bladder wall suggesting tumor extensions to the perivesical tissues and the left ureter (Fig. 1). There were no findings of distant metastasis. A serum hCG-β level was 0.3 ng/ml, slightly elevated (the normal range : $<$0.1 ng/ml). A total cystohysterectomy with an ileal conduit was performed in June 2005. Under histopathological examinations, a majority of the tumor consisted of syncytiotrophoblastic giant cells with necrosis and hemorrhage (Fig. 2). We evaluated the expression of hCG-β and human placental lactogen (hPL) in the cancerous tissue using immunohistochemistry. The tumor cells were found to be positive to anti-hCG-β, but negative to anti-hPL (Fig. 3). The final diagnosis was a primary choriocarcinoma of the urinary bladder, pT3a with metastases in right external lymph nodes. No tumor tissue was noted in the extirpated uterus. An adjuvant combination chemotherapy of methotrexate, vinblastine, adriamycin

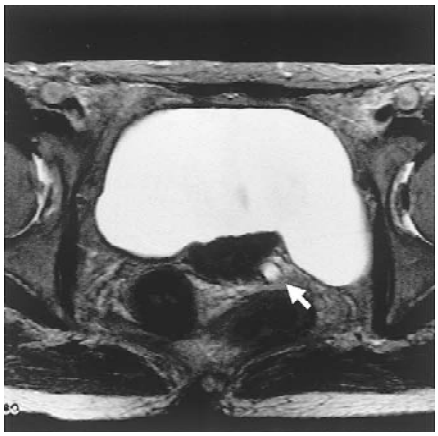

Fig. 1. Magnetic resonance imaging (MRI) revealed an irregular thickened bladder wall, which suggested that the lesion had extened to the perivesical tissues and left ureters (arrow).

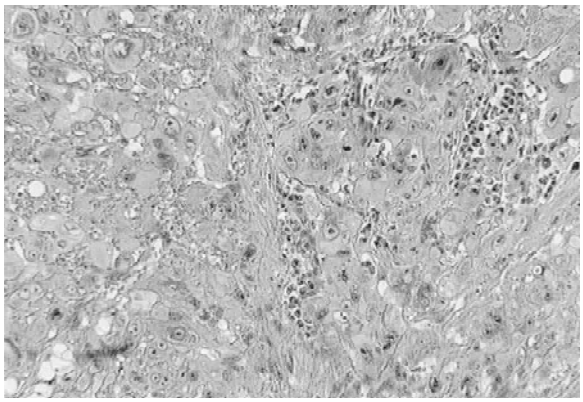

Fig. 2. Microscopically, a majority of tumor cells consist of syncytiotrophoblastic giant cells with necrosis and hemorrhage (hematoxylin and eosin stain; original magnification ×200).

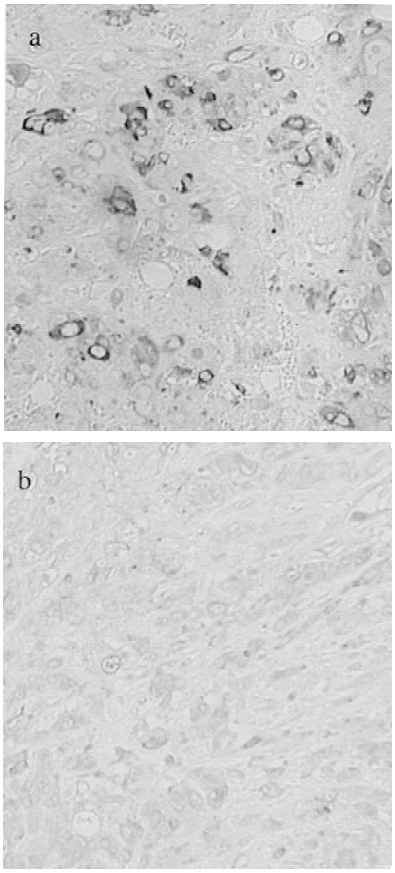

Fig. 3. Immunohistochemical analysis with anti-hCG-β and anti-hPL antibodies. (a) The tumor cells are positive for hCG-β, (b) but negative for hPL (Original magnification ×200).

and cisplatin (MVAC) was applied. After two cycles of the chemotherapy, the serum hCG-β level decreased to the normal range.

At 11 month follow-up, serum hCG-β level was found to have increased to 110.0 ng/ml, and she gradually developed dyspnea. Chest X-P revealed multiple lung metastases with pneumonia. A combination chemotherapy of cisplatin, etoposide and bleomycin (PEB) was planned, but the patient died of the disease at 12 months after the surgery. An autopsy was not performed.

DISCUSSION

Choriocarcinoma usually develops in the uterus and genital organs in the female. Its occurrence in the urinary bladder is relatively rare, as only 36 cases have so far been reported in the world[1–4]. According to the previous reports, there were 28 male and 8 female patients aged 19 to 82 years (mean 62.1 years). Masui et al. reported that primary choriocarcinoma of the urinary bladder is characterized as follows[5].: (i) histologically syntiotrophoblast-like cells are noted; (ii) hCG-β staining is positive in the tumor cells; (iii) the primary tumor lesion is absent from the testis, retroperitoneal space, mediastinum and pineal body. According to various reports, primary choriocarcinoma of the urinary bladder might be classified into two different categories: (i) in the course of development, germ cells in the state of suspended differentiation remain in the urogenital ridge to form the gonads, from which the carcinoma develops. In other words the tumor originates from germ cells and consists exclusively of choriocarcinoma components. Immunohistochemically, in addition, hPL staining is positive, and positivity to i(12p), a genetic marker, has also been reported. (ii) in the process of malignant transformation, the cancer cells change into giant cells that possess trophoblastic cell elements functionally as well as morphologically. Histologically ordinary urothelial carcinoma (UC) cells are usually mixed with the cancer cells; hPL staining is negative[3–7]. As indicated by previous reports containing clinical details[1–4], the tumor is either a histologically homogenous choriocarcinoma or a mixture with UC. When UC cells coexisted, in particular, it is suspected that the tumor is a metaplastic variant of UC. Of 36 cases, histological findings were documented in 33 cases; while pure choriocarcinoma was found in 8 cases (24.2%), the mixture of UC was seen in 25 cases (75.8%).

In our present series, no tumor was detected in other organs than urinary bladder; furthermore, immunohistochemical staining revealed hCG-β positive and hPL negative. These findings supported the diagnosis of metaplastic variant from UC. We then examined whether the difference in the tumor type affects the treatment policy and prognosis. Only two out of 8 cases with pure choriocarcinoma had survived until the time our investigation. The survival periods for two pure choriocarcinoma cases were 15 months and 33 months respectively[3–9]. As the initial treatment, TUR-Bt and/or total cystectomy were performed and systemic chemotherapy was used as an adjuvant, which was based on VAC (vincristine, actinomycin D and cyclophosphamide) or on BEP (bleomycin etoposide and cisplatin) in accordance with the standard therapy for

rhabdomyosarcoma and germ cell tumor. In contrast, in UC mixture cases, there is a survivor up to longest 20 months at the longest[3], and all cases died of cancer afterwards. Systemic chemotherapy based on MVAC (methotrexate, vinblastine, cisplatin, and adriamycin) is often employed in accordance with the standard therapy for ordinary bladder cancer. Though MVAC therapy provided a certain degree of an anti-cancer effect, there has been no report of complete remission in either other workers' cases or ours.

In our cases, serum hCG-β sharply rose after a temporary drop, accompanied by remote metastases. Thus, our patient followed clinical courses similar to those reported elsewhere. In addition, with special cases in which UC and micropapillary variant coexisted, there was the report that newly developed anti-cancer drugs, such as docetaxel and gemcitabine, were used[3]. This treatment was not found to have a sufficient anti-cancer effect, and the patients died from the progression of cancer. In summary, relatively long survival has been achieved by VAC therapy and/or BEP therapy in some pure choriocarcinoma. For metaplastic variant from UC, however, it is thought under the present conditions that there is no effective treatment including surgical treatment, radiotherapy and chemotherapy, even with recently developed carcinostatics. Further studies are warranted to identify a preferable treatment strategy including the use of new anti-cancer drugs for the poor prognosis of choriocarcinoma of the urinary bladder.

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和文抄録

原発性膀胱絨毛癌の1例

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症例は72歳の女性．肉眼的血尿のため受診．膀胱鏡では膀胱左側壁に invasive type，7 cm 大の腫瘍が認められた．経尿道的膀胱腫傷切除術を行ったところ病理組織学的には syncytiotrophoblastic giant cell が混在した未分化な尿路上皮癌の形態を示しG3，≧pT2 の結果であった．また血清 hCG-β は 0.3 ng/ml と上昇していた．MRI では膀胱周囲脂肪織および左尿管下端への浸潤が確認された．このため膀胱子宮全摘，回腸導管造設術を行った．最終的な病理診断は膀胱絨毛癌であった．術後 MVAC 療法を 2 クール実施し，hCG-β は基準値以下に低下したが11カ月目に多発性肺転移が出現し12カ月目に癌死した．

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